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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/129,298	08/05/98	ARNTZEN	C 7991-023-999

KIMERAGEN INC  
300 PHEASANT RUN  
NEWTOWN PA 18940

HM12/0315

EXAMINER

ZAGHMOUT, O

ART UNIT	PAPER NUMBER
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1649

DATE MAILED:

03/15/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.  
**09/129,298**

Applicant(s)  
**Arntzen et al.**

Examiner  
**Ousama Zaghmout**

Group Art Unit  
**1638**



☒ Responsive to communication(s) filed on Dec 29, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 1-4, 8-30, and 50-53 is/are pending in the application.

Of the above, claim(s) 28-30 and 50-53 is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1-4 and 8-27 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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### **STATUS OF APPLICATION**

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1638.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Response to restriction requirement:

Applicant's election with traverse of 1-4, 8-27 in Paper No. 12-29-99 is acknowledged. The traversal is on the ground(s) that the subject matter of claims 28-30 and 50-53 sufficiently related that of claims 1-4 and 8-27, to support the concurrent examination of these claims. This is not found persuasive because subject matter can be "related" and yet still be "independent" or patentability distinct. In the instant situation, the claimed method of Group I is both independent and patentability distinct. Clearly, they are independent since you could practice one invention, without practicing or infringing any of the others. Similarly, each is patentability distinct since they constitute different products which can each support its own patent..

The requirement is still deemed proper and is therefore made FINAL.

Claims 28-30, 5-53 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in Paper No. 8.

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4. Status of the claims:

The amendment filed 12-29-1999 have been received and entered (Paper No. 8).

Claims 1-4, 8-27 are considered on the merit.

Claims 1, 16, 28 and 50 have been amended.

Claims 5-7, 31-49 and 54-72 have been canceled.

Claims 1-4, 8-30, 50-53 are pending.

**Claim Rejections - 35 USC § 112**

**Ist paragraph**

1. Upon further consideration of the record, Applicants' arguments, and the declaration submitted by Dr. Walker, the rejection of these claims has been withdrawn.

**Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-4, 8-27 are rejected under 35 U.S.C. § 103 as being unpatentable over Kmiec et al [US patent number: 5,731,181. Date of publication: October 15, 1996] taken with Sanford et al [US patent number: 5,204,253; date of publication: April 20, 1993].

The claims are directed to a method of making a localized mutation in a target gene in a plant cell by adhering plant cells to a particle a recombinagenic oligonucleobase.

Kmiec et al teach a method for inducing alterations in targeted gene using recombinagenic oligonucleobase (Figure 1A and 1B) whereby a polynucleotide having both ribonucleotides and deoxyribonucleotides in a first strand and solely deoxyribonucleotides in a second strand; wherein the strands are Watson-Crick paired and are linked by an

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oligonucleotide so that the polynucleotide has at most a single 3' and a single 5' end. Kmiec et al teach that these ends can be ligated so that the polynucleotide is a single continuous circular polymer (fourth paragraph, column 1). Kmiec et al teach that in order to effect a genetic change, there are within the region of homology one or more non-corresponding (hereinafter "heterologous" or "mutator") base pairs. Kmiec et al teach that the normal, constitutive cellular processes of homologous recombination cause the mutator nucleotides to be inserted into the targeted genomic site. The duplex oligonucleotides (hereinafter "chimeric vectors") can be used to alter specifically a gene of interest by introducing into the gene the heterologous base pairs. Kmiec et al teach that the heterologous base pairs can be base pairs different from the gene of interest, or base pairs in addition to those present in the gene of interest (an insertion), or, lastly, the heterologous base pairs can be the absence of base-pairs found in the gene of interest (a deletion). Kmiec et al teach this method is based on part on the discovery that the inclusion of a region of between about 15 and 50 base pairs of hybrid-duplex nucleic acid in the vector causes a greatly increased rate of alteration of the gene of interest. Kmiec et al teach that when the region of the heterologous base pairs is between 1 and 50 base pairs, the heterologous base pairs can be present in the vectors of the invention as either a homo- or a hybrid-duplex. Kmiec et al teach that when the heterologous base pairs are greater than 50 base pairs in length it is preferred that they be present as a homo-duplex. Kmiec et al teach that the vector can be introduced into the target cell by any method known to allow for the introduction of nucleic acids into eukaryotic cells. Kmiec et al teach that without limitation as

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to theory, the chimeric vector is believed to be engaged by the recombination/repair mechanisms of the target cell and to direct a the alteration of the target gene by gene conversion or by homologous recombination (Column 3, lines 1-8 and column 4, lines 1-25). The reference teaches the transformation by electroporation (Example 6.2, columns 8 and 9)

Kmiec et al do not teach the adhering step is performed in a solution comprising 1.1-1.4 M NaCl and 18-22 uM spermidine and at least 14 ug/ml MDON.

Sanford et al a method for transformation of a number of plant species such as tobacco and peach (Example 3). Sanford et al teach the adhering step to tungsten particles which entails the use of 25 uL calcium chloride and 5 uL 0.1 M spermidine (paragraph 2, column 15). The reference teaches a method for transforming with a reporter gene, namely luciferase (Example 4, Table 7).

Given the recognition of those of ordinary skill in the art of the value of a developing a method for correcting genetic diseases that are mainly controlled by a single point mutation or to develop a method for screening transgenic plant containing the desirable traits, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teaching of Sanford et al for delivering by particle bombardment the genes taught by Kmiec et al, in order to produce a method for making localized mutation as claimed in the instant invention. Furthermore, the number of bases used in the sequence of the homologous

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or intervening regions, the choice of gene used, the method of adhering and transformation are a matter of choice unless the proof of criticality is provided. The use of different concentrations of spermidine or different salt such NaCl instead of CaCl<sub>2</sub> is a matter of choice unless the proof of criticality is provided. In addition, Applicants admit on the record that these conditions of particle bombardments are well known in the art (page 8 extending to page 9 of the specification). Plant cells transformed by the method of Sanford et al can easily be regenerated into plants using the teaching shown in Example 3 of Sanford et al's reference. Thus the claimed invention would have been prima facie obvious as a whole at the time it was made, especially in the absence of evidence to the contrary.

### Conclusion

No claims are allowed.



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**Future Correspondence**

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Ousama M-Faiz Zaghmout whose telephone number is (703) 308-9438. The Examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, L. Smith, can be reached on (703) 308-3909. The fax phone number for the group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to THE MATRIX CUSTOMER SERVICE CENTER whose telephone number is (703) 308-0196.

Ousama M-Faiz Zaghmout Ph.D.

March 10, 2000

ELIZABETH F. McELWAIN  
PRIMARY EXAMINER  
~~GROUP 1000~~

*Elizabeth F. McElwain*